

Aerospace Medicine Clinic

This article was prepared by Joseph J. Pavelites, B.S., Albert J. Lee, D.O., and Ricardo Ong, M.D.

You are a new military flight surgeon working at a military aviation medicine clinic. A voice message was left by a senior pilot stating that he completed his portion of his yearly physical months prior and got all his “GI (gastrointestinal) scopes”, but still has not been cleared to resume flying. You access the electronic medical record and notice that a physical examination with a waiver request was opened 8 mo ago but was never completed.

The patient is a 39-yr-old Caucasian male, military fixed-wing pilot. He is a half-pack-a-day smoker, is taking a proton pump inhibitor, and has had concerns for several years regarding chronic, frequent, loose stools. He does not endorse blood in his stool or symptoms of fatigue. His lab values—including a complete blood count, comprehensive metabolic panel, chest x-ray, and vitals—are within normal limits. His problem list reveals that he has several reasons for possibly needing an aeromedical waiver, including symptomatic gastroesophageal reflux disease, hiatal hernia, hereditary hemochromatosis, and mild chronic persistent asthma.

You are relieved to see that he has not been flying and there is proper documentation that he is currently not medically cleared for flight duties. However, as you dig deeper into the record, you also notice that there were photographs taken (see **Fig. 1**, **Fig. 2**, and **Fig. 3**) during his physical exam. The photographs reveal lesions that are confined to the arms and legs, palms of the hands, and bottom of the feet. Notes indicate that the patient raised concerns that he “has more [lesions] than he used to.” They are described as “blueish purple and compressible, and refill with blood quickly.” His physical exam is otherwise benign. He was sent for a venous ultrasound and referred to a gastrointestinal (GI) specialist for an extensive workup.

1. Examining the photo, the pilot most likely has which one of the following conditions?
 - A. Sturge-Weber Syndrome.
 - B. Blue rubber bleb nevus syndrome (BRBNS).
 - C. PHACE Syndrome (posterior fossa malformations, large facial hemangiomas, cerebral arterial anomalies, cardiovascular anomalies, and eye anomalies).
 - D. Gorham-Stout Disease.



Fig. 1. Tortuous venous malformations on the lateral heel of the left foot.

ANSWER/DISCUSSION

1. B. In BRBNS, the patient presents with venous malformations in the skin and/or the visceral organs. The venous malformations are described as blue to purple in color and can be

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Fig. 2. Tortuous venous malformations on the sole of the left foot.



Fig. 3. Tortuous venous malformations encircling the left proximal arm.

found throughout the skin; they also increase in number and size as the patient ages. The lesions are compressible and often hyperkeratotic.³ Sturge-Weber Syndrome is not the best answer as it presents with cutaneous capillary malformations of the face that are generally localized to the forehead and the upper eyelid.⁴ Similarly, PHACE syndrome is not a consideration as it has the hallmark of one or more facial hemangiomas seen in infancy.³ Gorham-Stout Syndrome is characterized by microcystic lymphatic malformation that infiltrates the bone. This results in osteolysis and cortical bone resorption.⁷ It does not fit the description of this flyer with a normal chest X-ray and venous malformations.

The chart mentions the previous flight surgeon's concern for the pilot having BRBNS. Curious to find out more about the syndrome and how it may impact safety of flight, you perform a literature search. You discover that BRBNS was first reported in 1860 and is a rare disorder with approximately 200 cases described in the literature.¹ Furthermore, BRBNS is caused by somatic double (cis) mutations in the TEK gene located on chromosome 9.^{3,6,11} You understand why a GI consult was ordered, as it appears the venous malformations of BRBNS frequently affect the GI system, often causing hemorrhage, iron-deficiency anemia, intussusception, and volvulus.^{3,6,11} Furthermore, the lesions may result in a wide range of clinical findings that include, but are not limited to, menorrhagia, intermittent proptosis, hematuria, epistaxis, hemoptosis, hemothorax, hemopericardium, and thrombotic

complications.⁸ If that is not enough of an aeromedical concern, these lesions have been shown to affect the central nervous system.⁵ The literature has reported cases of BRBNS having saccular (berry) aneurysms and multiple cavernoma-like lesions² that have led to fatal intracerebral hemorrhages and tuberous sclerosis complexes with unprovoked focal seizures, as well as additional cases with spasticity, ataxia, and weakness.¹

Looking at the results of his venous and GI studies, you see the ultrasound report documents several regions of the leg with nonpatent venous structures, including the left saphenous vein. Esophagogastroduodenoscopy results were notable for a gastric inlet patch and a 4.0 cm hiatal hernia. A tissue biopsy of erythematous gastric mucosa was negative for dysplasia and malignancy. An *H. pylori* stool Ag test was negative. The patient also underwent colonoscopy that was notable for granularity of the mucosa in the sigmoid colon and two polyps, with all the biopsies having no histopathology. Capsule endoscopy also did not contain evidence of BRBNS gastrointestinal lesions.

2. Which one of the following would be the next best test to perform as part of your risk mitigation strategy?
 - A. Fecal Occult Blood.
 - B. Lesion biopsy.
 - C. Genetic markers for BRBNS.
 - D. MRI of the brain.

ANSWER/DISCUSSION

2. **D.** As discussed previously, there have been cases where patients with BRBNS have also had associated central nervous system lesions with profound negative consequences.^{1,2,5} Because a full GI workup was performed, and the patient has normal complete blood count values, a fecal occult blood test is probably not the best test at this time. Though initially, once BRBNS is suspected, performing a fecal occult blood test would most certainly be recommended. With reasonable clinical evidence that BRBNS is present, a lesion biopsy and testing for genetic markers for the syndrome will not contribute significantly to managing aeromedical risk in the near-term. However, a biopsy was done on this patient with histopathology, revealing mildly tortuous vascular spaces of banal endothelial cells consistent with BRBNS, and referral to medical genetics is recommended for molecular confirmation of the diagnosis and better long-term risk management.

During your discussion with the patient, he asks about which treatment options, if any, he should consider for these asymptomatic cutaneous manifestations of the disease. Curious about treatments for BRBNS, you consult the literature.

3. Which one of the following is the best treatment for BRBNS, considering this patient's desire to fly and lack of GI manifestations?
 - A. Watchful waiting.
 - B. Sirolimus.
 - C. Sclerotherapy.
 - D. Vein therapy.

ANSWER/DISCUSSION

3. **A.** Watchful waiting. You do not have to treat the cutaneous manifestations if asymptomatic. B is not the best answer as asymptomatic cutaneous manifestation of BRBNS alone does not warrant treatment. However, several case reports depict successful treatment of symptomatic BRBNS lesions with sirolimus.^{10,12} Sirolimus is an immunosuppressant. While it might be an off-label option, this patient is not a good candidate since he has no active symptoms due to BRBNS. Choice C would be an option if the patient had GI complications of BRBNS. Sclerotherapy has been successful in treating of bleeding BRBNS lesions in the GI tract.^{6,9} Chemical sclerotherapy can be used for skin lesions, however it is not a necessary treatment for flight status. Vein therapy or resection are also options for treating individual lesions. However, again, removal of asymptomatic lesions will not directly benefit the patient for getting back on flight status.

While you await the results of the MRI, you review the various U.S. military services' waivers and Federal Aviation Administration guidance for arteriovenous malformations. As systemic arteriovenous malformations, such as BRBNS, are very rare, no specific guidance is given for aeromedical decision-making. The flight surgeon should apply the basic principles of aeromedical

decision-making when dealing with BRBNS and determine the qualification in conjunction with the appropriate aeromedical authority. The severity of the BRBNS symptoms and the potential for sudden or subtle incapacitation are important factors in making the aeromedical decision.

MRI results return with a disappointing finding of a saccular aneurysm in the Circle of Willis. Considering the lack of direct guidance from the various waiver guides, you decide to call your aeromedical approval authority for their opinion.

4. What is the best recommendation you will make to your aeromedical approval authority?
 - A. Waiver and return to full flight duties.
 - B. After treatment for the aneurysm, recommend return to full flight duties.
 - C. Permanent suspension of all flight duties.
 - D. No waiver necessary, submit a completed physical examination and return patient to full flight duties with the caveat that he needs to fly in a dual-piloted aircraft.

ANSWER/DISCUSSION

4. **C.** Considering the MRI findings and the progressive nature of the disease, it is best that he no longer flies. Although the risk of the aneurysm rupturing is not easily determined, the catastrophic result of such an event poses too much risk for this pilot to continue flying, making choice A unacceptable. Choice B is also unacceptable as BRBNS is a systemic condition and a dangerous aneurysm could appear at anytime, anywhere in the body. The patient would bring too much risk to himself, the crew, and the mission, even if he flew with another pilot.

After discussion with the proper aeromedical authorities, they agree that the pilot should be permanently suspended from all flight duties. You break the news to the pilot, set him up for further examination, and counsel him that retention in the military may not be a possibility.

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